

**REMARKS**

The Office Action mailed April 12, 2006, has been received and reviewed. Claims 7, 10, 11, 19-22, 24, 28-32, 34 and 36 are pending in the application and stand rejected. Claims 7, 19, 20, 22, 24, 29, 34 and 36 are amended herein. New claims 37-40 are added. No new matter is added. All amendments are made without prejudice or disclaimer. Reconsideration is respectfully requested. Applicants note that no grounds for rejection were stated for claims 21 and 36 and submit these claims are in condition for allowance.

**35 U.S.C. § 112, first paragraph**

Claims 22, 24, 28 and 31-32 stand rejected under 35 U.S.C. § 112, first paragraph. The Office Action states that the specification does not reasonably enable “a vaccine composition comprising an immunologically effective amount of any *Salmonella enterica* mutated bacterium.” (Office Action, mailed April 12, 2006, page 3). Instead, it was thought that the specification is only enabled for “vaccine compositions comprising an immunologically effective amount of a *Salmonella typhimurium STMP* mutated bacterium and a pharmaceutically acceptable carrier.” (Office Action, page 9).

More specifically, it was thought that the specification fails to enable “A) a vaccine comprising any mutated *Salmonella* bacterium from the group consisting of *Salmonella* species *typhimurium*, *enteritidis*, *choleraesuis*, *dublin*, *abortus-ovi*, *abortus-equii*, *derby*, *hadar*, *heidelberg*, *agona*, and *arizonae*, wherein said mutated bacterium lacking flagellin and wherein the vaccine is protective, B) a vaccine comprising any mutated *Salmonella* bacterium from the group consisting of *Salmonella* species *typhimurium*, *enteritidis*, *choleraesuis*, *dublin*, *abortus-ovi*, *abortus-equii*, *derby*, *hadar*, *heidelberg*, *agona*, and *arizonae*, wherein said mutated bacterium lacking flagellin and wherein the mutated bacterium is attenuated.” *Id.* Applicants note that claims 22, 24, 28 and 31-32 lack the Markush group described above.

Further, the Office Action repeats the citation of three references: Lockman et al., Wahden et al., and Hackett et al. At pages 4 to 6, the Office Action examines each of these references with the intent to show that the “skilled artisan is forced into undue experimentation to practice (make and use) the invention as it is broadly claimed because the prior art has taught that many strains of fla<sup>-</sup> are not protective, do not confer protection from subsequent challenge by

motile *Salmonella* bacteria and that mutations such as the flaF25 in the attenuation of *Salmonella* bacterium is unclear.” (Office Action at page 7, underlining in original).

Applicants respectfully affirm that the specification is enabling for the full scope of the instant claims without undue experimentation.

**A. The cited references fail to show that undue experimentation is necessary to practice the claimed invention.**

Regarding the cited references, Applicants assert that they fail to challenge the enablement of the claimed invention.

The Office Action characterizes Lockman as teaching “that flagella were necessary for *S. typhimurium* to invade and cause severe disease and the non-flagellated strains were equally proficient at colonization of the murine intestinal tract, but these mutants were deficient in invasion of the reticuloendothelial system.” (Office Action, page 4). It was further thought that Lockman shows that “*Salmonella* fla<sup>+</sup> (with flagella) bacteria are more likely to invade the host (e.g. reach the site of infection) than *Salmonella* fla- (non-motile or mutants wherein the mutated bacteria are not capable of inducing an immune response to at least one antigenic determinant of flagellin).” (Office Action at page 8).

However, in the quoted statement Lockman is referring to “previous investigations” which Lockman is challenging. Lockman actually teaches that, while flagella and motility play a role in the ability of *S. typhimurium* to infect **tissue culture monolayers *in vitro***, flagella are not a virulence factor of *in vivo* murine typhoid. (Lockman *et al.*, page 142, 1<sup>st</sup> column). Moreover, Lockman found that the lethal dose (LD<sub>50</sub>) of non-flagellated, non-motile *S. typhimurium* (fli-8007::Tn10) was nearly identical to that of the isogenic wild-type strains. *Id.* at 141, 2<sup>nd</sup> column. Accordingly, Lockman suggests that the presence or absence of flagella is irrelevant as a virulence factor for *Salmonella*. *Id.* at 142, 1<sup>st</sup> column.

Hackett is offered as allegedly showing a correlation between mice immunized with fla<sup>+</sup> *Salmonella* strains and protection from subsequent infection. (Office Action, page 8). Hackett was also cited to show that “a *S. typhimurium* M206 bacterium is not capable of inducing an immune response to at least one antigenic determinant of flagellin” and that “[o]ne of skill in the

art would not conclude that all strains of *Salmonella enterica* encompassed by the claimed invention are protective based on the teachings of the prior art.” (Office Action, page 8-9). However, Hackett teaches that multiple *fla<sup>+</sup>* strains do not confer protection—*S. typhimurium* M206 and *S. derby*. Additionally, in a discussion of Hackett, Lockman states that Hackett’s non-flagellated mutant (*flaF25*) has a “mutation that not only involves some of the genes encoding the biosynthesis of flagella, but extended into a previously undescribed virulence gene(s).” (See, Lockman at page 137, right column, lines 14-23).

Wahdan was also cited to show “there is a correlation between protection and H antigen” and that “the nonmotile mutant (lacking the H antigen) of *Salmonella typhi* did not protect against typhoid fever.” (Office Action, page 9). However, Wahdan acknowledges “[i]t seems more probable that a property other than the synthesis of the flagellar antigen determines immunogenicity and is absent from this non-motile motif.” (Wahdan, p. 72, right column, last lines). Moreover, it is uncertain that the 50 to 55 kDa protein discussed in Hackett is flagellin. Applicants also point out that that the *fla<sup>-</sup>* strains in Hackett still conferred protection against motile *Salmonella*, and Hackett expressly discloses that both *fla<sup>+</sup>* and *fla<sup>-</sup>* *Salmonella* strains induce cellular immunity—important in the defense against *Salmonella* infection. (Hackett, pages 82 and 83).

As such, Applicants respectfully assert, as was discussed in Lockman, Hackett, and Wahdan, that other factors are responsible for the lack of immunogenicity in Hackett, and not the absence of flagella.

As such, the cited references actually support the fact that non-flagellated and/or non-motile *Salmonella* were known to maintain virulence and to illicit a protective immune response *in vivo*. There is nothing in the cited prior art suggesting that any of the *Salmonella* serotypes encompassed by the claimed invention would not be protective. Therefore, the cited references fail to show that one of skill in the art would have required undue experimentation to make and use the claimed invention.

**B. The specification is enabling for a vaccine comprising a mutated *Salmonella enterica*.**

The specification would have allowed one of skill in the art to make and use the claimed

invention. Claims 22, 24, 28 and 31-32 herein contain in part the element of mutated *Salmonella enterica* bacteria. Those of skill in the art at the time of filing the instant application would have known that the genus *Salmonella* contains two species, each of which contains multiple serotypes. (Brenner FW, Villar RG, Angulo FJ, Tauxe R and B Swaminathan. *Salmonella* nomenclature. *Journal of Clinical Microbiology*, July 2000, p. 2465-2467). The two species are *S. enterica* and *S. bongori*. *S. enterica* is divided into six subspecies, the first being *S. enterica* subs. *enterica*. The subspecies contain serotypes usually named by the geographic location where they were first isolated, and grouped together because of their biochemical and genomic similarities. *Id.* at 2466. Many of the names for the serotypes are heterotypic synonyms, meaning that different names were given to the same bacterium. For example, it is generally accepted that *Salmonella enteritidis* and *Salmonella typhimurium* are heterotypic synonyms for *Salmonella enterica* subsp. *enterica*. Furthermore, the subspecies *S. enterica* subs. *enterica* includes the serotypes Typhimurium, Enteritidis, Choleraesuis, Dublin, Abortus-ovi, Abortus-equi, Derby, Hadar, Heidelberg and Agona. Accordingly, a reference to *S. enterica* is known by one of skill in the art, to include reference to the accompanying serotypes.

Moreover, for a claimed genus, such as *Salmonella enterica*, representative examples applicable to the genus as a whole are ordinarily enabling if one of skill in the art would expect the claimed genus could be used as disclosed in the specification without undue experimentation. (M.P.E.P. 2164.02). As such, the enablement of the claimed invention for a representative serotype of *S. enterica* subs. *enterica*, such as *S. typhimurium*, should be applicable and enabling to the other highly related or identical serotypes in the claimed invention.

Therefore, Applicants submit that because the instant specification is enabled for a vaccine composition for protection against Salmonellosis comprising an immunologically effective amount of *Salmonella typhimurium* STMP mutated bacteria (Office Action, page 2), which is a serotype and heterotypic synonym of *Salmonella enterica* subsp. *enterica*, the specification is also enabling for one of skill in the art to make and use the claimed invention for the other serotypes of *Salmonella enterica* subsp. *enterica*.

**C. Following the analysis in *In re Wands*, the specification is enabling for the claimed invention.**

To satisfy the enablement requirement, a specification must teach those skilled in the art how to make and use the scope of the claimed invention without undue experimentation. *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997). Furthermore, simulated or prophetic examples are permitted in patent applications (M.P.E.P., § 608.01(p)(II)) and the use of prophetic examples may make a patent enabling. *Atlas Powder Co. v. E.I. DuPont di Nemours & Co.*, 750 F.2d 1569, 1577 (Fed. Cir. 1984).

When determining undue experimentation, the PTO and the courts look to the factors outlined in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). The factors include 1) the quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and 8) the breadth of the claims.

In *In re Wands*, the United States Court of Appeals, Federal Circuit (CAFC) reversed a rejection for lack of enablement for an application claiming monoclonal hybridomas which secrete specific antibodies. *Id.* at 740. The CAFC found the disclosure of the Wands' patent application enabling because there was a high level of skill in the monoclonal antibody art and, despite the relative unpredictable nature of the technology, the patent disclosure provided guidance and real working examples of the invention. *Id.* at 738.

The CAFC recognized the complexity of the inventive technology but disagreed with the PTO, reasoning that the existing working examples, along with the specification, would allow one of ordinary skill in the art to make and use the invention. *Id.* at 740. The CAFC stated that a considerable amount of experimentation is permissible if it is reasonable with regards to the nature of the art or if the specification provides a reasonable amount of guidance. *Id.* at 737. The CAFC reasoned that the specification contained considerable direction and guidance on how to practice the claimed invention, presented working examples, that all the methods needed to practice the invention were well known, and that there was a high level of skill in the art at the time the application was filed. *Id.*

Following the analysis from *In re Wands*, the specification of the instant invention also would have allowed one of skill in the art to make and use the claimed invention without undue experimentation. The specification discloses detailed laboratory protocols and guidance for the

full scope of the claims, the referenced methods are well known by those of skill in the art, there are numerous fla- *Salmonella enterica* mutants known in the art, working examples are disclosed using *Salmonella enterica* serotypes, and the level of skill in the art was high at the time of filing.

**1. The specification includes working examples of non-flagellated mutant *Salmonella* marker vaccines in both chickens and pigs.**

The specification is enabling for the claimed invention because it includes working examples of non-flagellated mutant *Salmonella* marker vaccines in both chickens and pigs.

Specifically, Example 3 of the specification demonstrates that chickens vaccinated with a non-motile mutant of *S. typhimurium* STMP, called *S. typhimurium* STM2000, were protected against a wild-type challenge infection. All the STM2000 vaccinated chickens survived compared to an 80% death rate for those inoculated with a wild-type *S. typhimurium*. Thus demonstrating the successful immunogenicity of flagella-less *S. typhimurium* in chickens.

Example 4, at pages 22-23 of the specification, shows that the live attenuated flagella-less *S. typhimurium* STM2000 vaccine significantly reduced fecal shedding in pigs after a challenge infection with a wild-type *S. typhimurium* serotype. Thus demonstrating the successful immunogenicity of flagella-less *S. typhimurium* in pigs.

Another working example is provided by Example 2, at page 18 of the specification, which discloses vaccines comprising flagellated and non-flagellated *S. enteritidis*, specifically *S. enteritidis* fla<sup>+</sup> and *S. enteritidis* fla<sup>-</sup>. The results of Example 2 show that chickens vaccinated with the *S. enteritidis* fla<sup>-</sup> vaccines were negative for antibodies to the flagellin protein of *S. enteritidis* thus giving a clearly recognizable marker over those chickens vaccinated with the *S. enteritidis* fla<sup>+</sup> vaccine.

The specification also provides detailed instructions for selecting non-motile mutant from serotype *S. typhimurium* SL3261. (Example 1, page 17). In this example, a flagellin protein gene of *S. typhimurium* SL3261 was chemically mutagenized with NTG and non-motile mutants were selected by light microscopy. The selected mutant was named STM2001 and subsequent electrophoretic analysis revealed that the mutant lacked the flagellin protein fragment of 51kDa and pI 4.7, as compared to the non-mutant parent serotype. *Id.*

Furthermore, Applicants respectfully submit that it is not necessary to point out specific nucleotide mutations in the flagellin gene or biosynthesis pathway. Independent claims 7, 19, 22, 29 and 34 contain, in part, the element “wherein said live mutated bacterium is not capable of inducing an immune response to at least one antigenic determinant of flagellin in the subject to which it is administered.” The scope of the claims does not extend to a specific mutation but to a mutated phenotype wherein the mutated bacterium is not capable of inducing an immune response to at least one antigenic determinant of flagellin. The specification is clearly enabling for the process of mutating a *S. enterica* bacterium and for selecting the mutated phenotype. As such, it is not necessary to show which nucleotides are deleted, substituted or inserted.

Therefore, the instant specification provides multiple working examples of flagella-less and non-motile mutate *S. enterica* serotypes and would have allowed one of ordinary skill in the art to make and use effective marker vaccines.

**2. All the methods disclosed in the specification are well known in the art and the level of skill in the art was high at the time of filing the application.**

All the methods needed to practice the claimed invention are well known and there was a high level of skill in the art at the time the application was filed.

One of the disclosed methods is chemical mutagenesis, a technique well known in the art. (Specification, page 7, citing Andersen, P. 1995. *Mutagenesis*, p 31-58 in Methods in Cell Biology). For chemical mutagenesis of the flagellin gene or other known genes involved in the flagellum-biosynthesis pathway used by *S. enterica* serotypes, the bacterium are grown on blood agar selective medium and to the culture is added trioxalen (a commercially available chemical mutagen) and then the suspension is irradiated with U.V. 365 nm light. (Specification, page 15, example 1). Next, non-motile/flagella-less (fla-) mutants are easily selected with a light microscope by looking for a lack of motility and/or the absence of flagella. (Specification, page 7).

Using the chemical mutagenesis method, Applicants isolated a non-motile mutant of *S. typhimurium* STMP named STM2000. *Id.* In a different experiment following the same method, *S. typhimurium* SL3261 was chemically mutagenized with NTG. *Id.* at 17. The mutant STM2001 was isolated and found to have a specific flagellin mutation shown by the lack of the flagellin spot of 51kDa and pI 4.7, as compared to its parent strain. *Id.*

Alternatively, the specification outlines another standard method known in the art for fla-selection using monoclonal antibodies to select for bacteria lacking at least one antigenic determinant of flagellin. *Id.*

A second disclosed method allows for the introduction of a mutation at a predetermined nucleic acid site in a flagellin gene and/or a flagellum-biosynthesis gene. (Specification, page 8). This method relies on well-known recombinant DNA techniques by which the natural gene sequence may be disrupted or foreign DNA may be artificially introduced by homologous recombination such that the mutant cell survives but it is abnormal for the mutant gene product. (See, Alberts, B., Bray, D., Lewis, J., Raff, M., Roberts, K., Watson, J. D. Recombinant DNA Technology. In Molecular Biology of the Cell (B. Alberts, ed.), pp. 325-326. New York, Garland Publishing, Inc., 1994). The recombinant DNA techniques used in the construction of fla mutants are well-known standard techniques involving the cloning of the flagellin gene, modification of the gene sequence by site-directed mutagenesis, restriction enzyme digestion followed by reigation or PCR-approaches. (Specification, page 8 citing Sambrook, J. *et al.* Molecular Cloning: a laboratory manual. ISBN 0-8769-309-6). Furthermore, these recombinant DNA techniques may be performed using commercial recombination kits such as the Transformer® kit sold by Clonetech. (Specification, page 9).

The level of skill in the art is high, evidenced by the many genes and gene clusters involved in the flagellum-biosynthesis pathway that were described in the art. (Specification, page 6). In addition, the flagellin genes had been described for *S. enterica*, *S. enteritidis*, *S. dublin*, *S. typhimurium*, and *S. abortus-equi*. *Id.* Additionally, the flagellin genes of novel *Salmonella* species can easily be found using standard hybridization techniques based on homology with known *Salmonella* flagellin genes. *Id.*

The level of skill in the art at the time of filing is also evidenced by the disclosure of the reference Kutsukake *et al.* In Kutsukake, Mu d1(Ap<sup>r</sup> Lac) cts62 and Tn10 insertion mutants for

nearly all the flagellar genes in serotypes of *S. typhimurium* are disclosed. (Kutsukake *et al.*, pages 741-742). Kutsukake also discloses partial DNA sequence from flagellar operons of *S. typhimurium*. *Id.* at 745. As such, Kutsukake shows that there was detailed knowledge about the genes involved in the flagellar biosynthesis pathway allowing one of skill in the art to make and use the claimed invention without undue experimentation.

Despite the existence of numerous flagellar genes, there are only two flagellin protein genes in wild-type flagellum-bearing *Salmonella enterica* serotypes. *Id.* Of these two well known genes, only one is active and producing flagellin at a time. *Id.* As such, those of skill in the art could have readily constructed flagellin mutants by a routine mutagenesis of the two well known flagellin genes.

Therefore, the specification is enabling for the scope of the instant claims because, like in *In re Wands*, the recombinant DNA techniques are predictable and well known in the art, the specification provides significant and detailed guidance and includes real working examples applicable to the entire scope of the claimed invention.

For the reasons presented herein, applicants respectfully request removal of the rejection of claims 22, 24, 28 and 31-32 and ask reconsideration of the claims.

### 35 U.S.C. §102

A. Claims 7, 11, 22, 29, 30, 31 and 32 stand rejected under 35 U.S.C. §102(b) as anticipated by Joys *et al.* (Journal of General Microbiology, 1965, 41, 47-55). Applicants respectfully traverse the rejection.

It was thought that Joys teaches “compositions comprising fla- *Salmonella typhimurium* bacterium in broth culture.” (Office Action, page 10). However, Joys fails to disclose what would constitute “an immunologically effective amount of live mutated bacteria” as recited in independent claim 7. Further, Joys discloses that the fla- *Salmonella typhimurium* occurred due to spontaneous mutation. (Joys, Abstract). Thus, Joys fails to disclose the “live mutated bacteria are *Salmonella enterica* that in their wild-type form carried flagella having at least one antigenic determinant.” As these elements are not disclosed in Joys, claim 7 is not anticipated thereby.

Claim 11 is allowable at least for the same reason as claim 7. Further, M.P.E.P. 2143.01 explains that if “the proposed modification or combination of the prior art would change the

principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious.” (citing *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)). Further, “[i]f a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification.” (citing, *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)). Applicants respectfully submit that freeze-drying the *Salmonella* bacterial cultures, as suggested by the Office Action, would change the principle of operation of the Joy cultures, which are used for transduction studies performed by diluting broth cultures, thereby rendering the cultures unsatisfactory for their intended purpose of transduction studies. Accordingly, Joys cannot anticipate claim 11 of the presently claimed invention.

Claim 22 includes the element of “[a]n improved *Salmonella* vaccine, having an immunologically effective amount of *Salmonella enterica* bacteria and an adjuvant in a pharmaceutically acceptable carrier.” Applicants respectfully submit that Joys fails to disclose either a *Salmonella* vaccine or the presence of an adjuvant. Additionally, independent claim 22 includes the element of the “mutated bacteria being inactivated.” As these elements are not disclosed in Joys, claim 22 is not anticipated thereby.

Similarly, claim 29 includes the element “an immunologically effective amount of mutated *Salmonella enterica*” which is not disclosed in Joys. Further, Joys discloses that the fla-*Salmonella typhimurium* occurred due to spontaneous mutation. (Joys, Abstract). Thus, Joys fails to disclose the “wherein the wild type form of the mutated *Salmonella enterica* carried flagella having at least one antigenic determinant.” Additionally, Joys fails to disclose the presence of an adjuvant as recited in claim 29. As these elements are not disclosed in Joys, claim 29 is not anticipated thereby.

Claims 30, 31 and 32 are each allowable at least for the same reasons as claim 29. Reconsideration and withdrawal of the rejection is requested.

**B.** Claims 7, 11, 20, 22, 28, 29, 30, 31 and 32 stand rejected under 35 U.S.C. §102(b) as anticipated by Lockman et al. (*Infection and Immunity*, January 1990, p. 137-143). Applicants respectfully traverse the rejection.

It was thought that Lockman teaches “compositions comprising fla- *Salmonella typhimurium* bacterium in broth culture containing glucose.” (Office Action, page 12). However, Lockman fails to disclose what would constitute “an immunologically effective amount of live mutated bacteria” as recited in independent claim 7. As Lockman fails to disclose this element, it cannot anticipate the present invention.

Similarly, independent claims 20, 22 and 29 include the similar element of “an immunologically effective amount of live mutated *Salmonella typhimurium*” and Lockman fails to disclose this element. Additionally, it was stated that the non-flagellated strains of Lockman did not confer immunity. (Office Action, page 4). Thus, Lockman teaches away from the “immunogenic composition” of claim 7 and the compositions including “an immunologically effective amount of live mutated *Salmonella typhimurium*” as recited in claims 20, 22 and 29.

Claims 22 and 29 also include the similar recitation of “an adjuvant.” Applicants respectfully submit that Lockman fails to disclose either a *Salmonella* vaccine or the presence of an adjuvant. Additionally, with respect to independent claim 22, this claim includes the element of the “mutated bacterium being inactivated.” As these elements are not disclosed in Joys, claims 22 and 29 are not anticipated thereby. Reconsideration and withdrawal of the rejection is requested.

Claim 28 is allowable at least for the same reasons as independent claim 22.

Claims 30, 31, and 32 are each allowable at least for the same reasons as independent claim 29.

**C.** Claims 19, 22, 24, 28, 29, 30, 32 and 34 stand rejected under 35 U.S.C. §102(b) as anticipated by Wahdan et al. (Bull World Health Organ., Vol. 52, 1975). Applicants respectfully traverse the rejection.

By way of contrast with Wahdan, each of claims 19, 22, 24, 28, 29, 30, 32 and 34 include the similar element of “an immunologically effective amount of inactivated mutated bacteria, the inactivated mutated bacteria having a mutation in a gene encoding flagellin.” By contrast, Wahdan fails to disclose that the mutant strains have “a mutation in a gene encoding flagellin.” Support for the amendment may be found throughout the as-filed specification including, for

example, page 5. Accordingly, Wahdan cannot anticipate the presently claimed invention. Reconsideration and withdrawal of the rejection is requested.

**D.** Claims 19, 22, 24, 28, 29, 30, 32 and 34 stand rejected under 35 U.S.C. §102(b) as anticipated by Anderson (GB Patent No. 1,109,179). Applicants respectfully traverse the rejection.

By way of contrast with Anderson, each of claims 19, 22, 24, 28, 29, 30, 32 and 34 include the similar element of “an immunologically effective amount of inactivated mutated bacteria, the inactivated mutated bacteria having a mutation in a gene encoding flagellin.” By contrast, Anderson fails to disclose that the mutant strains have “a mutation in a gene encoding flagellin.” Accordingly, Anderson cannot anticipate the presently claimed invention. Reconsideration and withdrawal of the rejection is requested.

#### **New claims**

New claims 37-39 are added and find support throughout the as-filed specification, including claims 7 and 10 and page 12, lines 1-4. New claim 40 finds support in the as-filed specification, including claim 20. No new matter is added. Claims 37-40 avoid the cited art at least for the same reasons as stated herein.

**CONCLUSION**

In view of the foregoing, applicants respectfully request removal of the rejections and kindly ask reconsideration of the claims. Claims 7, 10, 11, 19-22, 24, 28-32, 34, and 36-40 are believed to be in condition for allowance and an early notice thereof is kindly requested. If questions remain after consideration of the foregoing, the Office is kindly requested to contact Applicants' attorney at the address or telephone number given herein.

Respectfully submitted,



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